CLAIMS

What is claimed:

1. A solid phase synthesis method for preparing a peptide-spacer-lipid conjugate, comprising the steps of:

(1) synthesizing an amino acid residue protected peptidyl resin in solid phase;

(2) conjugating a spacer and a lipid to the peptidyl resin, thereby forming a peptide-spacer-lipid resin having a peptide-spacer-lipid;

(3) cleaving the peptide-spacer-lipid from the peptide-spacer-lipid resin;

(4) removing at least one side chain protecting group from at least one amino acid of the peptide-spacer-lipid, thereby forming a peptide-spacer-lipid conjugate; and

(5) subjecting the peptide-spacer-lipid conjugate to a process selected from a group consisting essentially of:

(a) no further processing,

(b) modifying a peptide portion of the peptide-spacer-lipid conjugate to a cyclic form during any of the foregoing steps (1) – (4), and

(c) modifying a peptide portion of the peptide-spacer-lipid conjugate to a cyclic form after any of the foregoing steps (1) – (4).

2. The method, as recited in Claim 1, wherein the peptidyl resin comprises synthesizing by a process selected from a group consisting essentially of a Fmoc solid phase peptide synthesis technique and a Boc solid phase peptide synthesis technique.

3. The method, as recited in Claim 1, wherein the peptide-spacer-lipid resin comprises forming by conjugating a spacer to the peptidyl resin to obtain a spacer-peptidyl resin and by subsequently conjugating a lipid to the spacer-peptidyl resin.

4. The method, as recited in Claim 1, wherein the peptide-spacer-lipid resin comprises forming by conjugating a spacer-lipid to the peptidyl resin.

5. The method, as recited in Claim 1, wherein the spacer comprises a linear hydrophilic polymer chain.

6. The method, as recited in Claim 5, wherein the spacer comprises at least one compound selected from a group consisting essentially of polyglycine, polyethyleneglycol, polypropyleneglycol, polymethacrylamide, polydimethacrylamide, polyhydroxyethylacrylate, polyhydroxypropylmethacrylate, polyoxyalkene, and hydrophilic peptides.

7. The method, as recited in Claim 6, wherein the spacer comprises polyethylene glycol having a molecular weight in a range of approximately 100 to approximately 10,000 daltons.

8. The method, as recited in Claim 1, wherein the spacer comprises conjugating to a component selected from a group consisting essentially of the peptidyl resin and the lipid by a linkage functional group.

9. The method, as recited in Claim 8, wherein the linkage functional group comprises a component selected from a group consisting essentially of an amine, a urethane, an amide, a thio ester, and a thio ether.

10. The method, as recited in Claim 9, wherein the linkage functional group comprises an amide bond.

11. The method, as recited in Claim 10, wherein the amide bond comprises forming by an activating agent selected from a group consisting essentially of dicyclohexylcarbodiimide/N-hydroxybenzotriazole (DCC/HOBt), 1,3-diisopropylcarbodiimide/N-hydroxybenzotriazole (DIPCDI/HOBt), and 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide/N-hydroxysuccinimide (EDC/HOSu).

12. The method, as recited in Claim 10, wherein the amide bond comprises forming in at least one solvent selected from a group consisting essentially of DCM, $CHCl_3$, DMF, THF.

13. The method, as recited in Claim 10, wherein the amide bond comprises forming in a temperature range of approximately 20°C to approximately 90°C.

14. The method, as recited in Claim 10, further comprising the step of washing the peptide-spacer-lipid conjugate in a washing solution, wherein the washing solution comprises at least one solvent selected from a group consisting essentially of CH_2Cl_2, $CHCl_3$, MeOH, DMF, THF, HCN, H_2O, and at least one buffer.

15. The method, as recited in Claim 1, wherein the cyclic form of the peptide portion comprises forming by an intramolecular linkage between a pair of components selected from a group consisting essentially of two amino acids and at least one derivative of two amino acids.

16. The method, as recited in Claim 15, wherein the intramolecular linkage is selected from a group consisting essentially of disulfide, amide, ester, thioether, thioacetate, and thioacetamine.

17. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 1.

18. The peptide-spacer-lipid conjugate, as recited in Claim 17, wherein the peptide comprises a peptide ligand component selected from a group consisting essentially of a peptide ligand and peptide ligand mimetic.

19. The peptide-spacer-lipid conjugate, as recited in Claim 18, wherein the peptide ligand component is bound to a receptor.

20. The peptide-spacer-lipid conjugate, as recited in Claim 19, wherein the receptor is a component selected from a group consisting essentially of a somatostatin receptor, a vasoactive intestinal peptide receptor, an integrin receptor, a fibroblast growth factor receptor, a hepatocyte growth factor receptor, epidermal growth factor receptor, an insulin-like growth factor receptor, a nerve growth factor receptor, a vascular endothelial growth factor receptor, a platelet-derived growth factor receptor, and a transforming growth factor receptor.

21. The peptide-spacer-lipid conjugate, as recited in Claim 18, wherein the peptide ligand component comprises at least one material selected from a group consisting essentially of a hormone, a chemotaxin, a cytokine, a toxin, and a peptide of an extracellular matrix for cell adhesion.

22. The peptide-spacer-lipid conjugate, as recited in Claim 21, wherein the peptide ligand component comprises at least one material selected from a group consisting essentially of a somatostatin, vasoactive intestinal peptide, an integrin binding inhibitor, a fibroblast growth factor, a hepatocyte growth factor, an epidermal growth factor, a laminin binding inhibitor, a nerve growth factor, a fibronectin, a fibroblast growth factor, a insulin-like growth factor, a vascular endothelial growth factor, a platelet-derived growth factor, and a transforming growth factor.

23. The peptide-spacer-lipid conjugate, as recited in Claim 22, wherein the peptide ligand component comprises at least one material selected from the group consisting essentially of:

H-Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm)-OH,

H-Phe-Asn-Leu-Pro-Leu-Gly-Asn-Tyr-Lys-Lys-Pro-OH,

H-Leu-Gly-Thr-Ile-Pro-Gly-OH,

H-Gly-Arg-Gly-Glu-Ser-OH,

H-Glu-Ile-Leu-Asp-Val-OH,

H-Lys-Arg-Thr-Gly-Gln-Tyr-Lys-Leu-OH,

H-Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr-OH,

H-Gly-His-Lys-OH,

H-Pro-Glu-Ala-His-Trp-Thr-Lys-Leu-Gln-His-Ser-Leu-Asp-Thr-Ala-Leu-Arg-OH,

cyclic H- (D)Phe-Cys-Phe-(D)Trp-Lys-Thr-Cys-Thr(ol), and

cyclic H- (D)Phe-Cys-Phe-Gly-Lys-Thr-Cys-Thr(ol).

24. The peptide-spacer-lipid conjugate, as recited in Claim 17, wherein the lipid comprises a phospholipid selected from a group consisting essentially of a phosphodiglyceride and a sphingolipid.

25. A targeted therapeutic liposome comprising the peptide-spacer-lipid conjugate, as recited in Claim 17.

26. The targeted therapeutic liposome, as recited in Claim 25, wherein an agent component selected from a group consisting essentially of a therapeutic agent for

treating a disease and a diagnostic agent for diagnosing a disease, and wherein the agent component is entrapped.

27. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 2.

28. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 3.

29. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 4.

30. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 5.

31. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 6.

32. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 7.

33. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 8.

34. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 9.

35. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 10.

36. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 11.

37. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 12.

38. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 13.

39. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 14.

40. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 15.

41. A peptide-spacer-lipid conjugate synthesized by the method, as recited in Claim 16.